

```
=> e hinuma shuji/au
E1      6      HINUMA NOBUAKI/AU
E2     151     HINUMA S/AU
E3     259 --> HINUMA SHUJI/AU
E4      3      HINUMA SYUJI/AU
E5      1      HINUMA T/AU
E6      2      HINUMA TAKASATO/AU
E7      1      HINUMA TAKASHI/AU
E8      2      HINUMA TAKAYUKI/AU
E9      4      HINUMA TOMOAKI/AU
E10    630     HINUMA Y/AU
E11     2      HINUMA YASUKO/AU
E12    152     HINUMA YORIO/AU
```

```
=> s e3 and fpri?
L1      7 "HINUMA SHUJI"/AU AND FPRL?
```

```
=> dup rem l1
PROCESSING COMPLETED FOR L1
L2      5 DUP REM L1 (2 DUPLICATES REMOVED)
```

```
=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y
```

```
L2  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN
AN  2004:934582  CAPLUS
DN  141:388766
TI  Novel method of screening
IN  Kobayashi, Makoto; Habata, Yugo; Fujii, Ryo; Hinuma, Shuji
PA  Takeda Pharmaceutical Company Limited, Japan
SO  PCT Int. Appl., 146 pp.
    CODEN: PIXXD2
DT  Patent
LA  Japanese
FAN.CNT 1
```

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004095023	A1	20041104	WO 2004-JP5829	20040422
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	JP 2004340955	A	20041202	JP 2004-127118	20040422
	EP 1617216	A1	20060118	EP 2004-728959	20040422
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	US 2007009513	A1	20070111	US 2005-554234	20051021
PRAI	JP 2003-118760	A	20030423		
	WO 2004-JP5829	W	20040422		
AB	The use of a G-protein conjugated receptor protein containing an amino acid sequence identical with or substantially identical with the amino acid sequence of SEQ ID Number 1 or a salt thereof and a ligand peptide containing				
an	amino acid sequence represented by any of SEQ ID Nos. 3 to 7 or a salt thereof enables efficient screening of an agonist or antagonist for the above receptor protein or salt thereof.				

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:412964 CAPLUS
DN 140:400065
TI Novel FPRL1 ligands and use thereof
IN Hinuma, Shuji; Kobayashi, Makoto; Habata, Yugo; Harada,
Masataka; Okubo, Shoichi; Yoshida, Hiromi; Nishi, Kazunori
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041850	A1	20040521	WO 2003-JP14138	20031106
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003277575	A1	20040607	AU 2003-277575	20031106
	JP 2005034131	A	20050210	JP 2003-376376	20031106
	EP 1559721	A1	20050803	EP 2003-810620	20031106
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2007065819	A1	20070322	US 2005-534082	20051212
PRAI	JP 2002-324189	A	20021107		
	JP 2002-367119	A	20021218		
	JP 2003-59073	A	20030305		
	JP 2003-191359	A	20030703		
	WO 2003-JP14138	W	20031106		
AB	By using an FPRL1 ligand having an amino acid sequence which is the same or substantially the same as an amino acid sequence represented by SEQ ID NO:1, SEQ ID NO:17 or SEQ ID NO:21 together with FPRL1, an FPRL1 agonist or an FPRL1 antagonist can be efficiently screened.				

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:60796 CAPLUS
DN 140:105227
TI Novel screening method
IN Hinuma, Shuji; Fujii, Ryo; Harada, Masataka; Hosoya, Masaki; Mori, Masaaki
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004008141	A1	20040122	WO 2003-JP7501	20030612
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH,
 PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003242342 A1 20040202 AU 2003-242342 20030612

JP 2004121224 A 20040422 JP 2003-167341 20030612

PRAI JP 2002-205554 A 20020715

WO 2003-JP7501 W 20030612

AB Using a G protein-coupled receptor protein having an amino acid sequence which is the same or substantially the same as an amino acid sequence represented by SEQ ID NO:1, SEQ ID NO:17, SEQ ID NO:19 or SEQ ID NO:21 or its salt and a humanin-like peptide, a compound or a salt thereof capable of changing the binding properties of the above receptor protein or its salt to the humanin-like peptide can be efficiently screened.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 DUPLICATE 1

AN 2005:197900 BIOSIS

DN PREV200500191369

TI N-formylated humanin activates both formyl peptide receptor-like 1 and 2.

AU Harada, Masataka [Reprint Author]; Habata, Yugo; Hosoya, Masaki; Nishi, Kazunori; Fujii, Ryo; Kobayashi, Makoto; Hinuma, Shuji

CS Div Pharmaceut ResDiscovery Res Labs, Takeda Pharmaceut Co Ltd, 10 Wadai, Tsukuba, Ibaraki, 3004293, Japan
 Harada_Masataka@takeda.co.jp

SO Biochemical and Biophysical Research Communications, (November 5 2004)
 Vol. 324, No. 1, pp. 255-261. print.
 CODEN: BBRCA9. ISSN: 0006-291X.

DT Article

LA English

ED Entered STN: 25 May 2005

Last Updated on STN: 25 May 2005

AB We have discovered that humanin (HN) acts as a ligand for formyl peptide receptor-like 1 (FPRL1) and 2 (FPRL2). This discovery was based on our finding that HN suppressed forskolin-induced cAMP production in Chinese hamster ovary (CHO) cells expressing human FPRL1 (CHO-hFPRL1) or human FPRL2 (CHO-hFPRL2). In addition, we found that N-formylated HN (fHN) performed more potently as a ligand for FPRL1 than HN: in CHO-hFPRL1 cells, the effective concentration for the half-maximal response (EC50) value of HN was 3.5 nM, while that of fHN was 0.012 nM. We demonstrated by binding experiments using (125I)-W peptide that HN and fHN directly interacted with hFPRL1 on the membrane. In addition, we found that HN and fHN showed strong chemotactic activity for CHO-hFPRL1 and CHO-hFPRL2 cells. HN is known to have a protective effect against neuronal cell death. Our findings contribute to the understanding of the mechanism behind HN's function.
 Copyright 2004 Elsevier Inc. All rights reserved.

L2 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:1007152 CAPLUS

DN 140:55331

TI Humanin is a ligand for G protein-coupled N-formyl peptide receptors
 FPRL1 and FPRL2: use in drug screening, diagnosis, and
 therapy for neurodegenerative diseases

IN Hinuma, Shuji; Fujii, Ryo; Harada, Masataka; Hosoya, Masaki

PA Takeda Chemical Industries, Ltd., Japan

SO PCT Int. Appl., 160 pp.

CODEN: PIXXD2

DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003106683	A1	20031224	WO 2003-JP7500	20030612
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003242340	A1	20031231	AU 2003-242340	20030612
	JP 2004101509	A	20040402	JP 2003-167338	20030612
	EP 1514930	A1	20050316	EP 2003-733385	20030612
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005233326	A1	20051020	US 2004-517956	20041213
	US 7172876	B2	20070206		
PRAI	JP 2002-173798	A	20020614		
	JP 2002-205470	A	20020715		
	WO 2003-JP7500	W	20030612		
AB	Screening of compds. affecting the binding of humanin with its cognate receptors FPRL1 and FPRL2, and the use of the screened compds. as therapeutic agent for neurodegenerative diseases or brain diseases, or apoptosis inhibitor, are disclosed. Use of the FPRL1 or FPRL2 coding polynucleotides, or antibodies to those receptors as diagnostic agent for those diseases, is claimed. Alzheimer's disease associated protein humanin was found to be the ligand for G protein-coupled N-formyl peptide receptors FPR-like 1 (FPRL1), and FPR-like 2 (FPRL2).				

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> e kobayashi makoto/au

E1	6	KOBAYASHI MAKO/AU
E2	3	KOBAYASHI MAKOO/AU
E3	1004 -->	KOBAYASHI MAKOTO/AU
E4	36	KOBAYASHI MAMI/AU
E5	8	KOBAYASHI MAMIKO/AU
E6	1	KOBAYASHI MAMORI/AU
E7	122	KOBAYASHI MAMORU/AU
E8	2	KOBAYASHI MAMPEI/AU
E9	38	KOBAYASHI MANABU/AU
E10	25	KOBAYASHI MANAMI/AU
E11	1	KOBAYASHI MANORU/AU
E12	1	KOBAYASHI MAORU/AU

=> s e3 and fprl?

L3 5 "KOBAYASHI MAKOTO"/AU AND FPRL?

=> dup rem l3

PROCESSING COMPLETED FOR L3

L4 3 DUP REM L3 (2 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2004:934582 CAPLUS
 DN 141:388766
 TI Novel method of screening
 IN Kobayashi, Makoto; Habata, Yugo; Fujii, Ryo; Hinuma, Shuji
 PA Takeda Pharmaceutical Company Limited, Japan
 SO PCT Int. Appl., 146 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004095023	A1	20041104	WO 2004-JP5829	20040422
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	JP 2004340955	A	20041202	JP 2004-127118	20040422
	EP 1617216	A1	20060118	EP 2004-728959	20040422
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	US 2007009513	A1	20070111	US 2005-554234	20051021
PRAI	JP 2003-118760	A	20030423		
	WO 2004-JP5829	W	20040422		

AB The use of a G-protein conjugated receptor protein containing an amino acid sequence identical with or substantially identical with the amino acid sequence of SEQ ID Number 1 or a salt thereof and a ligand peptide containing an amino acid sequence represented by any of SEQ ID Nos. 3 to 7 or a salt thereof enables efficient screening of an agonist or antagonist for the above receptor protein or salt thereof.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2004:412964 CAPLUS
 DN 140:400065
 TI Novel FPRL1 ligands and use thereof
 IN Hinuma, Shuji; Kobayashi, Makoto; Habata, Yugo; Harada, Masataka; Okubo, Shoichi; Yoshida, Hiromi; Nishi, Kazunori
 PA Takeda Chemical Industries, Ltd., Japan
 SO PCT Int. Appl., 191 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041850	A1	20040521	WO 2003-JP14138	20031106
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,				

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003277575 A1 20040607 AU 2003-277575 20031106
 JP 2005034131 A 20050210 JP 2003-376376 20031106
 EP 1559721 A1 20050803 EP 2003-810620 20031106

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2007065819 A1 20070322 US 2005-534082 20051212

PRAI JP 2002-324189 A 20021107
 JP 2002-367119 A 20021218
 JP 2003-59073 A 20030305
 JP 2003-191359 A 20030703
 WO 2003-JP14138 W 20031106

AB By using an FPRL1 ligand having an amino acid sequence which is
 the same or substantially the same as an amino acid sequence represented
 by SEQ ID NO:1, SEQ ID NO:17 or SEQ ID NO:21 together with FPRL1
 , an FPRL1 agonist or an FPRL1 antagonist can be
 efficiently screened.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 DUPLICATE 1

AN 2005:197900 BIOSIS

DN PREV200500191369

TI N-formylated humanin activates both formyl peptide receptor-like 1 and 2.

AU Harada, Masataka [Reprint Author]; Habata, Yugo; Hosoya, Masaki; Nishi,
 Kazunori; Fujii, Ryo; Kobayashi, Makoto; Hinuma, Shuji

CS Div Pharmaceut ResDiscovery Res Labs, Takeda Pharmaceut Co Ltd, 10 Wadai,
 Tsukuba, Ibaraki, 3004293, Japan
 Harada_Masataka@takeda.co.jp

SO Biochemical and Biophysical Research Communications, (November 5 2004)
 Vol. 324, No. 1, pp. 255-261. print.
 CODEN: BBRCA9. ISSN: 0006-291X.

DT Article

LA English

ED Entered STN: 25 May 2005
 Last Updated on STN: 25 May 2005

AB We have discovered that humanin (HN) acts as a ligand for formyl peptide
 receptor-like 1 (FPRL1) and 2 (FPRL2). This discovery
 was based on our finding that HN suppressed forskolin-induced cAMP
 production in Chinese hamster ovary (CHO) cells expressing human
 FPRL1 (CHO-hFPRL1) or human FPRL2 (CHO-hFPRL2). In
 addition, we found that N-formylated HN (fHN) performed more potently as a
 ligand for FPRL1 than HN: in CHO-hFPRL1 cells, the effective
 concentration for the half-maximal response (EC50) value of HN was 3.5 nM,
 while that of fHN was 0.012 nM. We demonstrated by binding experiments
 using (125I)-W peptide that HN and fHN directly interacted with hFPRL1 on
 the membrane. In addition, we found that HN and fHN showed strong
 chemotactic activity for CHO-hFPRL1 and CHO-hFPRL2 cells. HN is known to
 have a protective effect against neuronal cell death. Our findings
 contribute to the understanding of the mechanism behind HN's function.
 Copyright 2004 Elsevier Inc. All rights reserved.

=> e habata yugo/au

E1 44 HABATA Y/AU
 E2 75 HABATA YOICHI/AU
 E3 64 --> HABATA YUGO/AU
 E4 6 HABATA YURIKO/AU
 E5 1 HABATAKE JUGO/AU
 E6 1 HABATEMARIAM SOLOMON/AU
 E7 1 HABATH THOMAS/AU

E8 3 HABATJOU JACQUES/AU
E9 1 HABATOV R/AU
E10 4 HABAU S/AU
E11 102 HABAU SHIGEKI/AU
E12 2 HABAUER G/AU

=> s e3 and fp1?

L5 5 "HABATA YUGO"/AU AND FPRL?

=> dup rem 15

PROCESSING COMPLETED FOR L5

L6 3 DUP REM L5 (2 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:934582 CAPLUS

DN 141:388766

TI Novel method of screening

IN Kobayashi, Makoto; Habata, Yugo; Fujii, Ryo; Hinuma, Shuji

PA Takeda Pharmaceutical Company Limited, Japan

SO PCT Int. Appl., 146 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004095023	A1	20041104	WO 2004-JP5829	20040422
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	JP 2004340955	A	20041202	JP 2004-127118	20040422
	EP 1617216	A1	20060118	EP 2004-728959	20040422
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	US 2007009513	A1	20070111	US 2005-554234	20051021
PRAI	JP 2003-118760	A	20030423		
	WO 2004-JP5829	W	20040422		

AB The use of a G-protein conjugated receptor protein containing an amino acid sequence identical with or substantially identical with the amino acid sequence of SEQ ID Number 1 or a salt thereof and a ligand peptide containing

an amino acid sequence represented by any of SEQ ID Nos. 3 to 7 or a salt thereof enables efficient screening of an agonist or antagonist for the above receptor protein or salt thereof.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:412964 CAPLUS

DN 140:400065

TI Novel FPRL1 ligands and use thereof

IN Hinuma, Shuji; Kobayashi, Makoto; Habata, Yugo; Harada,

Masataka; Okubo, Shoichi; Yoshida, Hiromi; Nishi, Kazunori
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041850	A1	20040521	WO 2003-JP14138	20031106
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003277575	A1	20040607	AU 2003-277575	20031106
	JP 2005034131	A	20050210	JP 2003-376376	20031106
	EP 1559721	A1	20050803	EP 2003-810620	20031106
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2007065819	A1	20070322	US 2005-534082	20051212
PRAI	JP 2002-324189	A	20021107		
	JP 2002-367119	A	20021218		
	JP 2003-59073	A	20030305		
	JP 2003-191359	A	20030703		
	WO 2003-JP14138	W	20031106		
AB	By using an FPRL1 ligand having an amino acid sequence which is the same or substantially the same as an amino acid sequence represented by SEQ ID NO:1, SEQ ID NO:17 or SEQ ID NO:21 together with FPRL1, an FPRL1 agonist or an FPRL1 antagonist can be efficiently screened.				

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1

AN 2005:197900 BIOSIS

DN PREV200500191369

TI N-formylated humanin activates both formyl peptide receptor-like 1 and 2.

AU Harada, Masataka [Reprint Author]; Habata, Yugo; Hosoya, Masaki;

Nishi, Kazunori; Fujii, Ryo; Kobayashi, Makoto; Hinuma, Shuji

CS Div Pharmaceut ResDiscovery Res Labs, Takeda Pharmaceut Co Ltd, 10 Wadai, Tsukuba, Ibaraki, 3004293, Japan

Harada_Masataka@takeda.co.jp

SO Biochemical and Biophysical Research Communications, (November 5 2004)

Vol. 324, No. 1, pp. 255-261. print.

CODEN: BBRCA9. ISSN: 0006-291X.

DT Article

LA English

ED Entered STN: 25 May 2005

Last Updated on STN: 25 May 2005

AB We have discovered that humanin (HN) acts as a ligand for formyl peptide receptor-like 1 (FPRL1) and 2 (FPRL2). This discovery was based on our finding that HN suppressed forskolin-induced cAMP production in Chinese hamster ovary (CHO) cells expressing human FPRL1 (CHO-hFPRL1) or human FPRL2 (CHO-hFPRL2). In addition, we found that N-formylated HN (fHN) performed more potently as a ligand for FPRL1 than HN: in CHO-hFPRL1 cells, the effective concentration for the half-maximal response (EC50) value of HN was 3.5 nM,

while that of fHN was 0.012 nM. We demonstrated by binding experiments using (125I)-W peptide that HN and fHN directly interacted with hFPRL1 on the membrane. In addition, we found that HN and fHN showed strong chemotactic activity for CHO-hFPRL1 and CHO-hFPRL2 cells. HN is known to have a protective effect against neuronal cell death. Our findings contribute to the understanding of the mechanism behind HN's function.
Copyright 2004 Elsevier Inc. All rights reserved.

=> e harada masataka/au

```
E1      1      HARADA MASASUMI/AU
E2      1      HARADA MASATA/AU
E3      68 --> HARADA MASATAKA/AU
E4      1      HARADA MASATAKU/AU
E5      3      HARADA MASATARO/AU
E6      61     HARADA MASATO/AU
E7      1      HARADA MASATO KISARAZU/AU
E8      35     HARADA MASATOMI/AU
E9      111    HARADA MASATOSHI/AU
E10     2      HARADA MASATSUNE/AU
E11     9      HARADA MASAYA/AU
E12     102    HARADA MASAYASU/AU
```

=> s e3 and fprl?

L7 6 "HARADA MASATAKA"/AU AND FPRL?

=> dup rem 17

PROCESSING COMPLETED FOR L7

L8 4 DUP REM L7 (2 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:412964 CAPLUS

DN 140:400065

TI Novel FPRL1 ligands and use thereof

IN Hinuma, Shuji; Kobayashi, Makoto; Habata, Yugo; Harada, Masataka
; Okubo, Shoichi; Yoshida, Hiromi; Nishi, Kazunori

PA Takeda Chemical Industries, Ltd., Japan

SO PCT Int. Appl., 191 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041850	A1	20040521	WO 2003-JP14138	20031106
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2003277575	A1	20040607	AU 2003-277575	20031106
	JP 2005034131	A	20050210	JP 2003-376376	20031106
	EP 1559721	A1	20050803	EP 2003-810620	20031106
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			

US 2007065819 A1 20070322 US 2005-534082 20051212
 PRAI JP 2002-324189 A 20021107
 JP 2002-367119 A 20021218
 JP 2003-59073 A 20030305
 JP 2003-191359 A 20030703
 WO 2003-JP14138 W 20031106

AB By using an FPRL1 ligand having an amino acid sequence which is the same or substantially the same as an amino acid sequence represented by SEQ ID NO:1, SEQ ID NO:17 or SEQ ID NO:21 together with FPRL1, an FPRL1 agonist or an FPRL1 antagonist can be efficiently screened.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2004:60796 CAPLUS
 DN 140:105227
 TI Novel screening method
 IN Hinuma, Shuji; Fujii, Ryo; Harada, Masataka; Hosoya, Masaki; Mori, Masaaki
 PA Takeda Chemical Industries, Ltd., Japan
 SO PCT Int. Appl., 116 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004008141	A1	20040122	WO 2003-JP7501	20030612
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003242342	A1	20040202	AU 2003-242342	20030612
JP 2004121224	A	20040422	JP 2003-167341	20030612
PRAI JP 2002-205554	A	20020715		
WO 2003-JP7501	W	20030612		

AB Using a G protein-coupled receptor protein having an amino acid sequence which is the same or substantially the same as an amino acid sequence represented by SEQ ID NO:1, SEQ ID NO:17, SEQ ID NO:19 or SEQ ID NO:21 or its salt and a humanin-like peptide, a compound or a salt thereof capable of changing the binding properties of the above receptor protein or its salt to the humanin-like peptide can be efficiently screened.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 DUPLICATE 1
 AN 2005:197900 BIOSIS
 DN PREV200500191369
 TI N-formylated humanin activates both formyl peptide receptor-like 1 and 2.
 AU Harada, Masataka [Reprint Author]; Habata, Yugo; Hosoya, Masaki; Nishi, Kazunori; Fujii, Ryo; Kobayashi, Makoto; Hinuma, Shuji
 CS Div Pharmaceut ResDiscovery Res Labs, Takeda Pharmaceut Co Ltd, 10 Wadai, Tsukuba, Ibaraki, 3004293, Japan
 Harada_Masataka@takeda.co.jp
 SO Biochemical and Biophysical Research Communications, (November 5 2004)
 Vol. 324, No. 1, pp. 255-261. print.

CODEN: BBRCA9. ISSN: 0006-291X.

DT Article
LA English
ED Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005
AB We have discovered that humanin (HN) acts as a ligand for formyl peptide receptor-like 1 (FPRL1) and 2 (FPRL2). This discovery was based on our finding that HN suppressed forskolin-induced cAMP production in Chinese hamster ovary (CHO) cells expressing human FPRL1 (CHO-hFPRL1) or human FPRL2 (CHO-hFPRL2). In addition, we found that N-formylated HN (fHN) performed more potently as a ligand for FPRL1 than HN: in CHO-hFPRL1 cells, the effective concentration for the half-maximal response (EC50) value of HN was 3.5 nM, while that of fHN was 0.012 nM. We demonstrated by binding experiments using (125I)-W peptide that HN and fHN directly interacted with hFPRL1 on the membrane. In addition, we found that HN and fHN showed strong chemotactic activity for CHO-hFPRL1 and CHO-hFPRL2 cells. HN is known to have a protective effect against neuronal cell death. Our findings contribute to the understanding of the mechanism behind HN's function. Copyright 2004 Elsevier Inc. All rights reserved.

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:1007152 CAPLUS
DN 140:55331
TI Humanin is a ligand for G protein-coupled N-formyl peptide receptors FPRL1 and FPRL2: use in drug screening, diagnosis, and therapy for neurodegenerative diseases
IN Hinuma, Shuji; Fujii, Ryo; Harada, Masataka; Hosoya, Masaki
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 160 pp.
CODEN: PIXXD2

DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003106683	A1	20031224	WO 2003-JP7500	20030612
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003242340	A1	20031231	AU 2003-242340	20030612
	JP 2004101509	A	20040402	JP 2003-167338	20030612
	EP 1514930	A1	20050316	EP 2003-733385	20030612
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005233326	A1	20051020	US 2004-517956	20041213
	US 7172876	B2	20070206		
PRAI	JP 2002-173798	A	20020614		
	JP 2002-205470	A	20020715		
	WO 2003-JP7500	W	20030612		

AB Screening of compds. affecting the binding of humanin with its cognate receptors FPRL1 and FPRL2, and the use of the screened compds. as therapeutic agent for neurodegenerative diseases or brain diseases, or apoptosis inhibitor, are disclosed. Use of the FPRL1 or FPRL2 coding polynucleotides, or antibodies to those receptors as diagnostic agent for those diseases, is claimed. Alzheimer's disease associated protein humanin was found to be the ligand for G

protein-coupled N-formyl peptide receptors FPR-like 1 (FPRL1),
and FPR-like 2 (FPRL2).

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> e ohkubo shoichi/au

E1	2	OHKUBO SHIZUYA/AU
E2	2	OHKUBO SHOHACHIRO/AU
E3	48 -->	OHKUBO SHOICHI/AU
E4	1	OHKUBO SHOWYA/AU
E5	3	OHKUBO SHUHEI/AU
E6	58	OHKUBO SHUICHI/AU
E7	6	OHKUBO SHUJI/AU
E8	1	OHKUBO SHUN SUKE/AU
E9	4	OHKUBO SHUNICHI/AU
E10	14	OHKUBO SHUNJI/AU
E11	1	OHKUBO SHUNSUKE/AU
E12	2	OHKUBO SHUICHI/AU

=> s e3 and fprl?

L9 0 "OHKUBO SHOICHI"/AU AND FPRL?

=> e yoshida hiromi/au

E1	1	YOSHIDA HIROM/AU
E2	12	YOSHIDA HIROMASA/AU
E3	558 -->	YOSHIDA HIROMI/AU
E4	139	YOSHIDA HIROMICHI/AU
E5	43	YOSHIDA HIROMITSU/AU
E6	1	YOSHIDA HIROMITU/AU
E7	85	YOSHIDA HIROMU/AU
E8	1	YOSHIDA HIROMUCHI/AU
E9	1	YOSHIDA HIRONAGA/AU
E10	2	YOSHIDA HIRONAO/AU
E11	2	YOSHIDA HIRONO/AU
E12	16	YOSHIDA HIRONOBU/AU

=> s e3 and fprl?

L10 1 "YOSHIDA HIROMI"/AU AND FPRL?

=> d

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:412964 CAPLUS

DN 140:400065

TI Novel FPRL1 ligands and use thereof

IN Hinuma, Shuji; Kobayashi, Makoto; Habata, Yugo; Harada, Masataka; Okubo, Shoichi; Yoshida, Hiromi; Nishi, Kazunori

PA Takeda Chemical Industries, Ltd., Japan

SO PCT Int. Appl., 191 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041850	A1	20040521	WO 2003-JP14138	20031106
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,				

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003277575 A1 20040607 AU 2003-277575 20031106
 JP 2005034131 A 20050210 JP 2003-376376 20031106
 EP 1559721 A1 20050803 EP 2003-810620 20031106

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2007065819 A1 20070322 US 2005-534082 20051212

PRAI JP 2002-324189 A 20021107
 JP 2002-367119 A 20021218
 JP 2003-59073 A 20030305
 JP 2003-191359 A 20030703
 WO 2003-JP14138 W 20031106

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> e nishi kazunori/au

E1 1 NISHI KAZUMA/AU
 E2 3 NISHI KAZUNOBU/AU
 E3 67 --> NISHI KAZUNORI/AU
 E4 51 NISHI KAZUO/AU
 E5 2 NISHI KAZURO/AU
 E6 1 NISHI KAZUTAKA/AU
 E7 19 NISHI KAZUTO/AU
 E8 24 NISHI KAZUYA/AU
 E9 20 NISHI KAZUYOSHI/AU
 E10 15 NISHI KAZUYUKI/AU
 E11 1 NISHI KEI/AU
 E12 13 NISHI KEIGO/AU

=> s e3 and fp1?

L11 4 "NISHI KAZUNORI"/AU AND FPRL?

=> dup rem l11

PROCESSING COMPLETED FOR L11

L12 2 DUP REM L11 (2 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:412964 CAPLUS

DN 140:400065

TI Novel FPRL1 ligands and use thereof

IN Hinuma, Shuji; Kobayashi, Makoto; Habata, Yugo; Harada, Masataka; Okubo,
 Shoichi; Yoshida, Hiromi; Nishi, Kazunori

PA Takeda Chemical Industries, Ltd., Japan

SO PCT Int. Appl., 191 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004041850	A1	20040521	WO 2003-JP14138	20031106
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,				

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003277575	A1	20040607	AU 2003-277575	20031106
JP 2005034131	A	20050210	JP 2003-376376	20031106
EP 1559721	A1	20050803	EP 2003-810620	20031106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2007065819	A1	20070322	US 2005-534082	20051212
PRAI JP 2002-324189	A	20021107		
JP 2002-367119	A	20021218		
JP 2003-59073	A	20030305		
JP 2003-191359	A	20030703		
WO 2003-JP14138	W	20031106		

AB By using an FPRL1 ligand having an amino acid sequence which is the same or substantially the same as an amino acid sequence represented by SEQ ID NO:1, SEQ ID NO:17 or SEQ ID NO:21 together with FPRL1, an FPRL1 agonist or an FPRL1 antagonist can be efficiently screened.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 1

AN 2005:197900 BIOSIS

DN PREV200500191369

TI N-formylated humanin activates both formyl peptide receptor-like 1 and 2.

AU Harada, Masataka [Reprint Author]; Habata, Yugo; Hosoya, Masaki; Nishi, Kazunori; Fujii, Ryo; Kobayashi, Makoto; Hinuma, Shuji

CS Div Pharmaceut ResDiscovery Res Labs, Takeda Pharmaceut Co Ltd, 10 Wadai, Tsukuba, Ibaraki, 3004293, Japan
Harada_Masataka@takeda.co.jp

SO Biochemical and Biophysical Research Communications, (November 5 2004)
Vol. 324, No. 1, pp. 255-261. print.
CODEN: BBRCA9. ISSN: 0006-291X.

DT Article

LA English

ED Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005

AB We have discovered that humanin (HN) acts as a ligand for formyl peptide receptor-like 1 (FPRL1) and 2 (FPRL2). This discovery was based on our finding that HN suppressed forskolin-induced cAMP production in Chinese hamster ovary (CHO) cells expressing human FPRL1 (CHO-hFPRL1) or human FPRL2 (CHO-hFPRL2). In addition, we found that N-formylated HN (fHN) performed more potently as a ligand for FPRL1 than HN: in CHO-hFPRL1 cells, the effective concentration for the half-maximal response (EC50) value of HN was 3.5 nM, while that of fHN was 0.012 nM. We demonstrated by binding experiments using (125I)-W peptide that HN and fHN directly interacted with hFPRL1 on the membrane. In addition, we found that HN and fHN showed strong chemotactic activity for CHO-hFPRL1 and CHO-hFPRL2 cells. HN is known to have a protective effect against neuronal cell death. Our findings contribute to the understanding of the mechanism behind HN's function.
Copyright 2004 Elsevier Inc. All rights reserved.

=> s fprl?

L13 681 FPRL?

=> dup rem l13

PROCESSING COMPLETED FOR L13

L14 374 DUP REM L13 (307 DUPLICATES REMOVED)

=> s l14 and agonist?

L15 99 L14 AND AGONIST?

=> s l15 and antibod?

L16 7 L15 AND ANTIBOD?

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):y

L16 ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2006:338564 BIOSIS
DN PREV200600337123
TI Annexin I regulates epithelial cell migration by signaling through formyl peptide receptors.
AU Babbin, Brian Alexander [Reprint Author]; Lee, Winston; Winfree, L. Matthew; Akyildiz, Adil; Parkos, Charles A.; Perretti, Mauro; Nusrat, Asma
CS Emory Univ, Atlanta, GA 30322 USA
SO FASEB Journal, (MAR 7 2006) Vol. 20, No. 5, Part 2, pp. A1093.
Meeting Info.: Experimental Biology 2006 Meeting. San Francisco, CA, USA. April 01 -05, 2006. Amer Assoc Anatomists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr; Amer Soc Pharmacol & Expt Therapeut.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 5 Jul 2006
Last Updated on STN: 5 Jul 2006
AB Annexin 1 (AnxA1) is a multifunctional phospholipid binding protein that has been identified as a metastasis-associated protein in a subset of epithelial malignancies. We hypothesize that AnxA1 regulates epithelial cell migration/invasion. Mechanisms by which annexin I regulates epithelial cell motility are unknown. To analyze the role of AnxA1 in regulating epithelial cell migration, we used a model epithelial cell line (SKCO-15) derived from colorectal adenocarcinoma. Localization studies revealed the presence of AnxA1 on the Surface of SKCO-15 cells which was increased upon the induction of cell migration. Functionally, neutralizing AnxA1 antibodies significantly inhibited SKCO-15 cell migration through matrigel-coated filters. Conversely, SKCO-15 cell migration was increased in the presence of the AnxA1 peptide mimetic, Ac2-26. Since extracellular AnxA1 has been shown to regulate leukocyte migratory events through interactions with n-formyl peptide receptors (nFPRs), we documented expression of FPR-1, FPRL-1, and FPRL-2 in SKCO-15 cells by RT-PCR and Western blot analysis. Ac2-26, and the classical nFPR agonist, fMLP, stimulated intracellular calcium release consistent with nFPR activation. The Ac2-26-induced intracellular calcium release and increase in SKCO-15 cell invasion was abrogated by the nFPR antagonist, Boc2. Together, these results support an autocrine/paracrine role for membrane annexin I in regulating SKCO-15 cell migration through nFPR signaling.

L16 ANSWER 2 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2006:329125 BIOSIS
DN PREV200600326748
TI Annexin 1 and its bioactive peptide inhibit neutrophil-endothelium interactions under flow: indication of distinct receptor involvement.
AU Hayhoe, Richard P. G.; Kamal, Ahmad M.; Solito, Egle; Flower, Roderick J.; Cooper, Dianne; Perretti, Mauro [Reprint Author]
CS Barts and London Queen Mary Sch Med and Dent, William Harvey Res Inst, Ctr Biochem Pharmacol, Charterhouse Sq, London EC1M 6BQ, UK
m.perretti@qmul.ac.uk
SO Blood, (MAR 1 2006) Vol. 107, No. 5, pp. 2123-2130.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Article

LA English
ED Entered STN: 28 Jun 2006
Last Updated on STN: 28 Jun 2006
AB We have tested the effects of annexin 1 (ANXA1) and its N-terminal peptide Ac2-26 on polymorphonuclear leukocyte (PMN) recruitment under flow. Differential effects of the full-length protein and its peptide were observed; ANXA1 inhibited firm adhesion of human PMNs, while Ac2-26 significantly attenuated capture and rolling without effect on firm adhesion. Analysis of the effects of ANXA1 and Ac2-26 on PMN adhesion molecule expression supported the flow chamber results, with Ac2-26 but not ANXA1 causing L-selectin and PSGL-1 shedding. ANXA1 and its peptide act via the FPR family of receptors. This was corroborated using HEK-293 cells transfected with FPR or FPRL-1/ALX (the 2 members of this family expressed by human PMNs). While Ac2-26 bound both FPR and FPRL-1/ALX, ANXA1 bound FPRL-1/ALX only. ANXA1 and Ac2-26 acted as genuine agonists; Ac2-26 binding led to ERK activation in both FPR- and FPRL-1/ALX-transfected cells, while ANXA1 caused ERK activation only in cells transfected with FPRL-1/ALX. Finally, blockade of FPRL-1/ALX with a neutralizing monoclonal antibody was found to abrogate the effects of ANXA1 in the flow chamber but was without effect on Ac2-26-mediated inhibition of rolling. These findings demonstrate for the first time distinct mechanisms of action for ANXA1 and its N-terminal peptide Ac2-26.

L16 ANSWER 3 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2004:154408 BIOSIS
DN PREV200400155979
TI A truncated form of CKbeta8-1 is a potent agonist for human formyl peptide-receptor-like 1 receptor.
AU Elagoz, Aram [Reprint Author]; Henderson, Duncan; Babu, Poda Suresh; Salter, Sylvia; Grahames, Caroline; Bowers, Lorna; Roy, Marie-Odile; Laplante, Patricia; Grazzini, Eric; Ahmad, Sultan; Lembo, Paola M. C.
CS AstraZeneca R and D Montreal, 7171 Frederick-Banting, Ville Saint-Laurent, Saint Laurent, PQ, H4S 1Z9, Canada
aram.elagoz@astrazeneca.com
SO British Journal of Pharmacology, (January 2004) Vol. 141, No. 1, pp. 37-46. print.
ISSN: 0007-1188 (ISSN print).

DT Article
LA English
ED Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB 1 Human formyl peptide-receptor-like-1 (FPRL-1) is a promiscuous G protein-coupled receptor (GPCR), and belongs to a chemoattractant receptor family protein. This receptor has been reported to interact with various host-derived peptides and lipids involved in inflammatory responses. We described here, a novel role for FPRL-1 as a high-affinity beta-chemokine receptor for an N-terminally truncated form of the CKbeta8 (CCL23/MPIF-1) splice variant CKbeta8-1 (22-137 aa). 2 RT-PCR analysis of mRNA derived from human tissues and cells revealed a predominant expression of FPRL-1 in inflammatory cells, particularly in neutrophils. 3 Intracellular calcium mobilisation assay, used as screening tool, in recombinant Chinese hamster ovary (CHO-K1) and human embryonic kidney (HEK293s) cells coexpressing FPRL-1 and Galpha16, demonstrated FPRL-1 is a functional high-affinity receptor for CKbeta8-1 (46-137 aa, sCKbeta8-1), with pEC50 values of 9.13 and 8.85, respectively. 4 The FPRL-1 activation in CHO-K1 cells is mediated by Galphai/Galphao proteins, as assessed by pertussis toxin sensitivity and inhibition of forskolin-induced cyclic AMP accumulation. 5 Binding experiments were performed with a radio-iodinated synthetic peptide, (125-I)-WKYMVm, a known potent FPRL-1 agonist. CHO-K1 cell membranes expressing FPRL-1 bound (125-I)-WKYMVm with a Kd value of 9.34. Many known FPRL-1 agonists were tested and sCKbeta8-1 was the most effective nonsynthetic ligand in

displacing the radiolabelled agonist, with a pIC₅₀ of 7.97. 6
The functional significance of sCKbeta8-1 interaction with FPRL
-1 was further demonstrated by the activation of polymorphonuclear
leukocytes (PMNs) calcium mobilisation and chemotaxis. These interactions
were shown to be via FPRL-1 by specific blockade of PMNs
activation in the presence of an FPRL-1 antibody.

L16 ANSWER 4 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2002:203857 BIOSIS
DN PREV200200203857
TI The fibrinolytic receptor for urokinase activates the G protein-coupled
chemotactic receptor FPRL1/LXA4R.
AU Resnati, M.; Pallavicini, I.; Wang, J. M.; Oppenheim, J.; Serhan, C. N.;
Romano, M.; Blasi, F. [Reprint author]
CS Molecular Genetics Unit, Department of Cell Biology and Functional
Genomics, DIBIT-Istituto Scientifico San Raffaele and Universita
Vita-Salute San Raffaele, Via Olgettina 58, 20132, Milano, Italy
blasi.francesco@hsr.it
SO Proceedings of the National Academy of Sciences of the United States of
America, (February 5, 2002) Vol. 99, No. 3, pp. 1359-1364. print.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
LA English
ED Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002
AB The function of urokinase and its receptor is essential for cell migration
in pathological conditions, as shown by the analysis of knockout mice
phenotypes. How a protease of a fibrinolytic pathway can induce migration
is not understood and no link between this protease and
migration-promoting G protein-coupled receptors has been described. We
now show that FPRL1/LXA4R, a G protein-coupled receptor for a
number of polypeptides and for the endogenous lipoxin A4 (LXA4), is the
link between urokinase-type plasminogen activator (uPA) and migration as
it directly interacts with an activated, soluble, cleaved form of uPA
receptor (uPAR) (D2D388-274) to induce chemotaxis. In this article we
show that (i) both uPAR and FPRL1/LXA4R are necessary for the
chemotactic activity of uPA whereas FPRL1/LXA4R is sufficient to
mediate D2D388-274-induced cell migration. (ii) Inhibition or
desensitization of FPRL1/LXA4R by antibodies or
specific ligands specifically prevents chemotaxis induced by D2D388-274 in
THP-1 cells and human peripheral blood monocytes. (iii) Desensitization of
FPRL1/LXA4R prevents the activation of tyrosine kinase Hck induced
by D2D388-274. (iv) D2D388-274 directly binds to FPRL1/LXA4R and
is competed by two specific FPRL1/LXA4R agonists, the
synthetic MMK-1 peptide and a stable analog of LXA4. Thus, a naturally
produced cleaved form of uPAR is a unique endogenous chemotactic
agonist for FPRL1/LXA4R receptor and its activity can be
antagonized by specific ligands. These results provide the first direct
link, to our knowledge, between the fibrinolytic machinery and the
inflammatory response, demonstrating that uPA-derived peptide fragments
can activate a specific chemotactic receptor.

L16 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:412964 CAPLUS
DN 140:400065
TI Novel FPRL1 ligands and use thereof
IN Hinuma, Shuji; Kobayashi, Makoto; Habata, Yugo; Harada, Masataka; Okubo,
Shoichi; Yoshida, Hiromi; Nishi, Kazunori
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041850	A1	20040521	WO 2003-JP14138	20031106
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003277575	A1	20040607	AU 2003-277575	20031106
	JP 2005034131	A	20050210	JP 2003-376376	20031106
	EP 1559721	A1	20050803	EP 2003-810620	20031106
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2007065819	A1	20070322	US 2005-534082	20051212
PRAI	JP 2002-324189	A	20021107		
	JP 2002-367119	A	20021218		
	JP 2003-59073	A	20030305		
	JP 2003-191359	A	20030703		
	WO 2003-JP14138	W	20031106		

AB By using an FPRL1 ligand having an amino acid sequence which is the same or substantially the same as an amino acid sequence represented by SEQ ID NO:1, SEQ ID NO:17 or SEQ ID NO:21 together with FPRL1, an FPRL1 agonist or an FPRL1 antagonist can be efficiently screened.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:1007152 CAPLUS
DN 140:55331
TI Humanin is a ligand for G protein-coupled N-formyl peptide receptors
FPRL1 and FPRL2: use in drug screening, diagnosis, and therapy for neurodegenerative diseases
IN Hinuma, Shuji; Fujii, Ryo; Harada, Masataka; Hosoya, Masaki
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003106683	A1	20031224	WO 2003-JP7500	20030612
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003242340	A1	20031231	AU 2003-242340	20030612
	JP 2004101509	A	20040402	JP 2003-167338	20030612
	EP 1514930	A1	20050316	EP 2003-733385	20030612
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005233326	A1	20051020	US 2004-517956	20041213

US 7172876 B2 20070206
PRAI JP 2002-173798 A 20020614
JP 2002-205470 A 20020715
WO 2003-JP7500 W 20030612

AB Screening of compds. affecting the binding of humanin with its cognate receptors FPRL1 and FPRL2, and the use of the screened compds. as therapeutic agent for neurodegenerative diseases or brain diseases, or apoptosis inhibitor, are disclosed. Use of the FPRL1 or FPRL2 coding polynucleotides, or antibodies to those receptors as diagnostic agent for those diseases, is claimed. Alzheimer's disease associated protein humanin was found to be the ligand for G protein-coupled N-formyl peptide receptors FPR-like 1 (FPRL1), and FPR-like 2 (FPRL2).

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1997:196043 CAPLUS

DN 126:291403

TI Lipoxin A4 stable analogs are potent mimetics that stimulate human monocytes and THP-1 cells via a G-protein-linked lipoxin A4 receptor

AU Maddox, Jane F.; Hachicha, Mohamed; Takano, Tomoko; Petasis, Nicos A.; Fokin, Valery V.; Serhan, Charles N.

CS Cent. Exp. Therapeut. Reperfusion Injury, Brigham and Women's Hosp. and Harvard Med. Sch., Boston, MA, 02115, USA

SO Journal of Biological Chemistry (1997), 272(11), 6972-6978
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Lipoxins (LX) are bioactive eicosanoids that activate human monocytes and inhibit neutrophils. LXA4 is rapidly converted by monocytes to inactive products, and to resist metabolism, synthetic analogs of LXA4 were designed. Here, the authors examined the bioactivity of several LXA4 analogs in monocytes and found, for chemotaxis, 15(R/S)-methyl-LXA4 were equal in activity, and 16-phenoxo-LXA4 was more potent than native LXA4. Both 15(R/S)-methyl-LXA4 and 16-phenoxo-LXA4 were approx. 1 log molar more potent than LXA4 in stimulating THP-1 cell adherence ($EC_{50} \approx 1 + 10^{-10}$ M). Dimethylamide derivs. of the LXA4 analogs also possessed agonist rather than antagonist properties for monocytes. Neither LXA4 nor 16-phenoxo-LXA4 affected monocyte-mediated cytotoxicity. The authors cloned an LXA4 receptor from THP-1 cells identical to that found in PMN. Evidence of receptor-mediated function of LXA4 and the stable analogs in monocytes included desensitization of intracellular calcium mobilization to a second challenge by equimolar concns. of these analogs, but not to LTB4. Increases in $[Ca^{2+}]_i$ by LXA4 and the analogs were specifically inhibited by an antipeptide antibody to the LXA4 receptor; and both LXA4- and analog-induced adherence and increments in Ca^{2+} were sensitive to pertussis toxin. Together, these results indicate that the LXA4 stable analogs are potent monocyte chemoattractants and are more potent than native LXA4 in stimulating THP-1 cell adherence, at subnanomolar concns. Moreover, they provide addnl. evidence that the LXA4 stable analogs retain selective bioactivity in monocytes and are valuable instruments for examining the functions and modes of action of LXA4.